Docket No.	:	LATTA.002C3	**Customer No.: 20,995**
Application No.	:	10/660,924	
Filing Date	:	September 12, 2003	

REPLY BRIEF

Applicant	:	Paul P. Latta
App. No	:	10/660,924
Filed	:	September 12, 2003
For	:	PREVENTION OF DIABETES THROUGH INDUCTION OF IMMUNOLOGICAL TOLERANCE
Examiner	:	Belyavskyi, Michail
Art Unit	:	1644

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
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Sir:

In response to the Examiner's answer mailed January 27, 2006, Applicant submits this Reply Brief.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. The Examiner has rejected Claims 2-9 under 35 U.S.C. §112, first paragraph for lack of enablement. In particular, the Examiner has maintained that the Specification and the Declarations by Dr. Scharp showing efficacy of the claimed method in preventing type I diabetes in a mouse model of diabetes (non-obese diabetic, NOD mice) are not predictive of the outcome of using the claimed method for the prevention of Type I diabetes in human.

2. The Examiner has also rejected Claims 2-9 under 35 U.S.C. §112, first paragraph as having New Matter.

ARGUMENT

1. The Examiner has maintained rejections of Claims 2-9 under 35 USC §112, first paragraph, as being non-enabling for a method of preventing onset of Type I diabetes in a

mammal. In the Examiner's answer, the Examiner continued to insist on applying a much stricter standard than required by law. As discussed in Appellant's brief, MPEP 2107.03 explicitly states that evidence need not "be in the form of data from an art-recognized animal model for the particular disease or disease condition to which the asserted utility relates. . . .Thus, if one skilled in the art would accept the animal tests as being reasonably predictive of utility in humans, evidence from those tests should be considered sufficient to support the credibility of the asserted utility."

In the present case, Appellant submitted two Declarations of Dr. David Scharp showing that a significant percentage of the NOD mice receiving the treatment described in the specification were indeed prevented from becoming diabetic. Appellant also submitted a number of references from other scientists having ordinary skill in the art to establish the validity of the NOD mouse model in connection with human diabetes. The NIH state that the "NOD mouse, which spontaneously develops type 1 diabetes, is a valuable animal model that is used extensively in research exploring the etiology, prevention, and treatment of this disease. It is a vital research tool for testing promising prevention and treatment strategies at the preclinical level."[1] Furthermore, Hanninen et al. states: "The non-obese diabetic (NOD) mouse is the most widely used animal model of T1DM. . . research in non-obese diabetic mice has led to the discovery of new strategies of diabetes prevention that are now in human clinical trials".[2] The authors further presented a whole list of current clinical trials based on strategies developed in NOD mice[3].

According to MPEP 2107.02(VII), "evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true." (Emphasis in original.) The Examiner is required to "review the original disclosure,

[1] http://www.niaid.nih.gov/dait/NODmice.htm.
[2] Hanninen et al. 2003 "Development of new strategies to prevent type I diabetes: the role of animal models" *Annals of Medicine* **35**:546-563: page 546, right column, last paragraph through page 547, left column.
[3] *Id.*, Table 2.

any evidence relied upon in establishing the *prima facie* showing, any claim amendments, and any new reasoning or evidence provided by the applicant in support of an asserted specific and substantial credible utility." MPEP 2107.02(VI). However, rather than reviewing all of Appellant's evidence as required by the MPEP, the Examiner relied solely on other references which tended to raise doubts about the ability of the use of the NOD mouse model to predict effects in human disease. Relying on these references without even acknowledging Appellant's countervailing evidence is clear error that should be reversed on appeal.

The only acknowledgement of Appellant's evidence in the Examiner's Answer is where the Examiner states that "Contrary to Appellant's assertion, it is noted that the data presented in the declarations of Dr. Scharp under 37 CFR 1.132 clearly indicates that using NOD mice as a model, 40% of the treated animals developed diabetes." However, this information is not contrary to Appellant's assertion. The data provided in these declarations are in complete support of the Appellant's assertion that claimed method can be used in connection with treatment of diabetes in a mammal, because it shows that actually 60% of treated mice were prevented from becoming diabetic, while 100% of the control animals became diabetic. Therefore, there is a reasonable correlation to the asserted utility.

Therefore, using the proper standard set forth in the MPEP, the evidence provided by Applicant clearly supports that one skilled in the art would accept the NOD model as reasonably correlating to the condition in human. Accordingly, the rejection of Claims 2-9 as non-enabled is clearly improper.

2. The Examiner has improperly rejected Claims 2-9 for allegedly containing New Matter. Specifically, The Examiner has stated that the limitation added to Claim 2: "wherein said dose is at least one order of magnitude less than that necessary to achieve normoglycemia in a mammal of the same species with type I diabetes" is not supported by the passages of the Specification pointed to by the Applicant.

In the Examiner's answer, the Examiner states that the passages provided by the Appellant in support for the added limitation are contrary to the Appellant's assertion of support,

because the Specification originally "only disclosed two-step process, wherein a tolerizing dose is one or two orders of magnitude less than the curative in the method pf treating diabetes" (see page 11 of the Examiner's Answer). This statement is incorrect; the Specification as filed clearly establishes at page 10, line 21 that "a one-step process of implanting only a tolerizing dose" is contemplated. Then, at page 4, lines 26-27, the specification clearly states that "the tolerizing dose is one or two orders of magnitude less than the curative dose", while at page 9, line 9-11, the specification also clearly states that "[a]s for the bolus tolerizing dose, the incremental tolerizing dose is typically one or two orders of magnitude lower than the curative dose." Thus, the specification clearly establishes that the dose for prevention of diabetes is "at least one order of magnitude less than that necessary to achieve normoglycemia in a mammal of the same species with type I diabetes." Therefore, there is clear support in the Specification as filed for Claim 2, and its rejection over "New Matter" is improper.

Conclusion

In view of the arguments presented, Appellants submit that the Specification as filed enables a person with an ordinary skill in the art on how to make and use the invention. Appellants further submit that Claims 2-9 are fully supported by the Specification as filed and do not constitute New Matter.

March 27, 2006

Respectfully submitted,

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CLAIMS APPENDIX

1. **(Canceled)**

2. **(Previously presented)** A method of preventing onset of Type I diabetes in a mammal predisposed to Type I diabetes, comprising implanting a dose of insulin-producing cells encapsulated in a biologically-compatible membrane into an implantation site in said mammal prior to onset of Type I diabetes, wherein said dose is at least one order of magnitude less than that necessary to achieve normoglycemia in a mammal of the same species with type I diabetes.

3. **(Previously presented)** The method of Claim 2, wherein said cells are from a primary cell source.

4. **(Previously presented)** The method of Claim 3, wherein said cells are pancreatic islet cells.

5. **(Previously presented)** The method of Claim 2, wherein said cells are encapsulated in a conformal coating.

6. **(Previously presented)** The method of Claim 5, wherein said conformal coating comprises polyethylene glycol (PEG).

7. **(Previously presented)** The method of Claim 2, wherein the insulin-producing cells are from the same species as the mammal.

8. **(Previously presented)** The method of Claim 2, wherein Type I diabetes is prevented without continuous immunosuppression.

9. **(Previously presented)** The method of Claim 2, wherein the cells are implanted intraperitoneally.